UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/998,904	11/30/2001	Harold R. Garner	UTSW:1045RCE	4132

34725 7590 08/14/2008

CHALKER FLORES, LLP
2711 LBJ FRWY
Suite 1036
DALLAS, TX 75234

EXAMINER	
RIGGS II, LARRY D	

ART UNIT	PAPER NUMBER
1631	

MAIL DATE	DELIVERY MODE
08/14/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/998,904	GARNER ET AL.	
	Examiner	Art Unit	
	LARRY D. RIGGS II	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 April 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,5-7,9-42,44-53,56,57,203 and 204* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3, 5-7, 9-42, 44-53, 56-57, 203 and 204* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendments filed 09 April 2008 are acknowledged and entered.

Status of Claims

Claims 1-3, 5-7, 9-42, 44-53, 56-57, 203 and 204 are currently pending and under consideration.

Withdrawn Rejections/Objections

The objection of the amendment filed 15 October 2007 for introducing new matter, in the Office action mailed 09 January 2008 is withdrawn in view of the amendment and explanation filed 09 April 2008.

The rejection of claims 1-3, 5-7, 9-42, 44-53, 56-57, 203 and 204 under 35 U.S.C. 112, Second Paragraph, in the Office action mailed 09 January 2008 is withdrawn in view of the amendments filed 09 April 2008.

Claim Objections

Claims 18 and 19 are objected to because of the following informalities:

Claim 18 provides "wherein the of two or more genes" in line 1. It is suggested that applicant add "dataset" to provide the result "wherein the dataset of two or more genes" as recited in the previous dependent claims, to result in grammatical correctness.

Claim 19 provides "wherein the of two or more genes" in line 1. It is suggested that applicant add "dataset" to provide the result "wherein the dataset of two or more genes" as recited in the previous dependent claims, to result in grammatical correctness.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-3, 5-7, 9-42, 44-53, 56-57, 203 and 204 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

The instant claims are drawn to a method and a computer program for predicting one more locations of single nucleotide polymorphisms in a nucleic acid sequence.

Since the claimed invention involves mathematical algorithm, which is a judicial exception, the following analysis of facts of this particular patent application follows the rationale suggested in the "Interim Guidelines for Examination of Patent Applications for Patent Subject Matter Eligibility" (OG Notices: 22 November 2005, available from the US PTO website at http://www.uspto.gov/web/offices/com/sol/og/2005/week47/og200547.htm).

The Guidelines states:

> *To satisfy section 101 requirements, the claim must be for a practical application of the § 101 judicial exception, which can be identified in various ways (Guidelines, p. 19):*
>
> *- The claimed invention "transforms" an article or physical object to a different state or thing.*

- The claimed invention otherwise produces a useful, concrete and tangible result.

In the instant claims, there is no physical transformation by the claimed invention, because calculating a variation frequency, generating a variation predictiveness matrix, comparing a nucleic acid sequence with the matrix, identifying locations of probable polymorphisms and outputting the identified polymorphisms are not physical transformations. Thus the Examiner must determine if the instant claims produce a useful, tangible, and concrete final result.

In determining if the instant claims have a useful, tangible, and concrete final result, the Examiner must determine each standard individually. For a claim to be "useful", the claim must produce a final result that is specific, substantial and credible. For a claim to be "tangible", the claim must set forth a practical application of the invention that produces a real-world final result. For a claim to be "concrete", the process must have a final result that can be substantially repeatable or the process must substantially produce the same result again. Furthermore, the claim must recite a useful, tangible, and concrete final result in the claim itself, and the claim must be limited only to statutory embodiments. Thus if the claim is broader than the statutory embodiments of the claim, the Examiner must reject the claim as non-statutory.

Method claims 1-3, 5-7, 9-42, 44-53, 56-57 do not produce a tangible final result. A tangible requirement requires that the claim must set forth a practical application of the database to produce a real-world result. The instant claims are drawn to a method of predicting SNPs in a nucleic acid sequence. However, the last step of the claims

include outputting the identified locations of the single nucleic acid polymorphisms to a computer display, an electronic file or a printer. There is no guarantee that a user will have access to the electronic file, or understand the data encoded on the electronic file. Since the claim itself must include a useful, concrete and tangible final result, the instant claims are non-statutory.

This rejection could be overcome by amendment of the claims to recite that a specific final result of the process is outputted to a user, or by including a result that is a physical transformation. The applicants are cautioned against introduction of new matter in an amendment.

Claims 203 and 204 are drawn to a computer readable medium comprising a computer program for predicting one or more locations of variations in a sequence. While the instant specification does not explicitly define the scope of the limitation of "computer readable medium," one skilled in the art would understand that computer readable medium includes carrier wave, which is a signal. For example, Fiekowsky et al., in US patent 6,090,555 (Date of Patent: July 18, 2000), define computer readable medium as being "a CD-ROM, floppy disk, tape, flash memory, system memory, hard drive, and a data signal embodied in a carrier wave." See column 14, claim 12. Bornstein et al., in US patent 6,1443,88 (Date of patent : Nov. 7, 2000) state, "The computer readable medium of the present invention generally includes a tape, a floppy disk, a CD ROM, a carrier wave. In a preferred embodiment, however, the computer readable medium of the present invention is a carrier wave." See column 8, lines 33-37.

Therefore, at least one embodiment of the instant claims 203 and 204 are drawn to carrier wave or a signal encoded thereon a computer program.

It was held by the court that claims that recite nothing but the physical characteristics of a form of energy, such as a frequency, voltage, or the strength of a magnetic field, define energy or magnetism, per se, and as such, are nonstatutory natural phenomena. O'Reilly, 56 U.S. (15 How.) at 112-14. Moreover, it does not appear that a claim reciting a signal encoded with functional descriptive material, e.g. a computer program, falls within any of the categories of patentable subject matter set forth in § 101. Likewise, a claim reciting only a signal does not appear to be a process, machine, manufacture, or composition of matter. See, e.g., In re Nuitjen, Docket no. 2006-1371 (Fed. Cir. Sept. 20, 2007)(slip. op. at 18)("A transitory, propagating signal like Nuitjen's is not a process, machine, manufacture, or composition of matter.' ... Thus, such a signal cannot be patentable subject matter."). The following analysis on why such a signal encoded with functional descriptive material is nonstatutory subject matter is excerpted from the US PTO's "Interim Guidelines for Examination of Patent Applications for Patent Subject Matter Eligibility" (OG Notices: 22 November 2005, available from the US PTO website at http://www.uspto.gov/web/offices/com/sol/og/2005/week47/og200547.htm):

> *First, a claimed signal is clearly not a "process" under § 101 because it is not a series of steps. The other three § 101 classes of machine, compositions of matter and manufactures "relate to structural entities and can be grouped as 'product' claims in order to contrast them with process claims." 1 D. Chisum, Patents §1.02 (1994. The three product classes have traditionally required physical structure or material.*

"The term machine includes every mechanical device or combination of mechanical device or combination of mechanical powers and devices to perform some function and produce a certain effect or result." Corning v. Burden, 56 U.S. (15 How.) 252, 267 (1854). A modern definition of machine would no doubt include electronic devices which perform functions. Indeed, devices such as flip-flops and computers are referred to in computer science as sequential machines. A claimed signal has no physical structure, does not itself perform any useful, concrete and tangible result and, thus, does not fit within the definition of a machine.

A "composition of matter" "covers all compositions of two or more substances and includes all composite articles, whether they be results of chemical union, or of mechanical mixture, or whether they be gases, fluids, powders or solids." Shell Development Co. v. Watson, 149 F. Supp. 279, 280, 113 USPQ 265, 266 (D.D.C. 1957), aff'd, 252 F.2d 861, 116 USPQ 428 (D.C. Cir. 1958). A claimed signal is not matter, but a form of energy, and therefore is not a composition of matter.

The Supreme Court has read the term "manufacture" in accordance with its dictionary definition to mean 'the production of articles for use from raw or prepared materials by giving to these materials new forms, qualities, properties, or combinations, whether by hand-labor or by machinery." Diamond v. Chakrabarty, 447 U.S. 303, 308, 206 USPQ 193, 196-97 (1980) (quoting American Fruit Growers, Inc. v. Brogdex Co., 283 U.S. 1, 11, 8 USPQ 131, 133 (1931), which, in turn, quotes the Century Dictionary). Other courts have applied similar definitions. See American Disappearing Bed Co. v. Arnaelsteen, 182 F. 324, 325 (9th Cir. 1910), cert. denied, 220 U.S. 622 (1911). These definitions require physical substance, which a claimed signal does not have. Congress can be presumed to be aware of an administrative or judicial interpretation of a statute and to adopt that interpretation when it re-enacts a statute without change. Lorillard v. Pons, 434 U.S. 575, 580 (1978). Thus, Congress must be presumed to have been aware of the interpretation of manufacture in American Fruit Growers when it passed the 1952 Patent Act.

A manufacture is also defined as the residual class of product. 1 Chisum, § 1.02[3] (citing W. Robinson, The Law of Patents for Useful Inventions 270 (1890)). A product is a tangible physical article or object, some form of matter, which a signal is not. That the other two product classes, machine and composition of matter, require physical matter is evidence that a manufacture was also intended to require physical matter. A signal, a form of energy, does not fall within either of the two definitions of manufacture. Thus, a signal does not fall within one of the four statutory classes of § 101.

These interim guidelines propose that such signal claims are ineligible for patent protection because they do not fall within any of the four statutory classes of § 101. Public comment is sought for further evaluation of this question.

Thus, claims 203 and 204 are drawn to nonstatutory subject matter.

Response to Arguments

Applicant's arguments filed 09 April 2008 have been fully considered and are persuasive in part.

Regarding the amended method claims 1-3, 5-7, 9-42, 44-53, 56-57, applicants argue that the specification and cancelled claim 210 discloses, the present invention "generates a delimited file suitable for standard spreadsheet application". Applicants argue that under MPEP § 2163.07(a), the use of computer displays, electronic files and printers with computers and computer implemented methods are common knowledge, well known to those skilled in the art and inherent. This argument is persuasive.

However, the amended method claims still do not provide a tangible result, because at least one embodiment of the claims, outputting the identified locations of the polymorphisms to an electronic file. A user would not necessarily have access to an electronic file, or understand the data of an electronic file.

Regarding amended claims 203 and 204, applicants argue that the claims do not claim a signal because "computer readable medium encoded with a computer program" has been determined to be statutory pursuant to MPEP § 2106.01(I)(second paragraph). Because the amended claims are directed toward statutory subject matter, the claims overcome the rejection under 35 U.S.C. § 101.

This argument is not persuasive.

Applicant's attention is drawn to the entire section of 2106.01 of the MPEP. Almost at the very beginning (second paragraph) of the section, the MPEP states that "[w]hen functional descriptive material is recorded on some computer-readable medium, it becomes structurally and functionally interrelated to the medium and will be statutory in most cases since use of technology permits the function of the descriptive material to be realized." (Emphases are added by the examiner.) It is conceivable that one of the reasons why such phrases as "some" and "in most cases" are used is that certain computer readable medium in certain cases will not be statutory even if encoded with functional descriptive material, such as a carrier wave. As set forth in the previous Office action and reiterated above, a claim reciting only a signal, (at least one embodiment of claims 203 and 204), does not appear to be a process, machine, manufacture, or composition of matter. See, e.g., In re Nuitjen, Docket no. 2006-1371 (Fed. Cir. Sept. 20, 2007)(slip. op. at 18)("A transitory, propagating signal like Nuitjen's is not a process, machine, manufacture, or composition of matter.' ... Thus, such a signal cannot be patentable subject matter.").

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 45 and 46 are rejected under 35 U.S.C. 102(b) as being anticipated by Shapiro et al. (Journal of Immunology, 1999, 163, 259-268).

The instant claim 1 provides a computer-implemented method for predicting one or more locations of single nucleotide polymorphisms in a nucleic acid sequence, comprising the steps of: calculating a variation frequency from a first base to a second base within a group of bases in a dataset of two or more genes; generating a variation predictiveness matrix from the calculated variation frequency; comparing the nucleic acid sequence, one or more bases in the nucleic acid sequence at a time, with the variation predictiveness matrix to assign a variation value to the one or more bases in the nucleic acid sequence; identifying the locations of the one or more bases in the nucleic acid sequence where single nucleotide polymorphisms will likely occur based on the assigned variation value; and outputting the identified locations of the single nucleotide polymorphisms to a computer display, an electronic file or a printer.

Regarding claim 1, Shapiro et al. shows oligonucleotide mutability indexes between bases, i.e. the number of times given a oligonucleotide within a segment of DNA contained a mutation divided by the number of times the oligonucleotide was expected to be mutated, (page 260, left column, last paragraph – right column, first paragraph; Tables I and II). Shapiro et al. shows a predicted composite mutability index for a region or nucleotides by determining the number of times each di- or trinucleotide occurred within each region of each gene and multiplying by its mutability index, (page 260, right column, second paragraph). Shapiro et al. shows comparing nucleic acid sequences with a composite regional mutability index, providing regions that would be

most (mutability indexes >1) or least mutable, CDR1 and CDR2 in both murine and human V_H genes were predicted to mutate the most, wherein these regions of predicted regional mutability are displayed (page 263; Figures 3-4; Table III).

Regarding claim 45, Shapiro et al. shows oligonucleotide mutability indexes between bases within bases from one to three at a time, (Tables 2-3).

Regarding claim 46, Shapiro et al. shows mutability indexes normalized for codon usage (page 260, right column, first and second paragraphs, pages 267-268; Figure 7).

Claim Rejections – 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in Graham v. John Deere Co., 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 2, 3, 5-7, 9, 10 and 37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shapiro et al. (Journal of Immunology, 1999, 163, 259-268), as applied to claims 1, 45 and 46 above, in view of Levy et al. (J. Exp. Med., 1988, 168, 475-489).

The instant claims 2-3 depend from claim 1 with the extra limitation that the nucleic acid sequence further comprises one or more chemical modifications including methylation or other chemical groups. The instant claims 5-6 depend from claim 1 with the extra limitation that a variation from the first base to the second base is nonsynonymous or synonymous. The instant claims 7, 9-10 depend from claim 1 with the extra limitation of a data set of SNPs or genes with chemical modifications. The instant claims 37-38 depend from claim 1 with the extra limitation that the nucleic acid comprises cDNA or a genomic sequence.

Shapiro et al. is applied to claim 1 above. Shapiro et al. does not show nucleic acid sequence further comprises one or more chemical modifications, variations from the first base to the second base being nonsynonymous or synonymous, data set of SNPs or genes with chemical modifications, or nucleic acid comprises cDNA, or a genomic sequence.

Regarding claims 2 and 3, Levy et al. shows the nucleic acid sequence of V region genes containing methylation at the cytosine residues, e.g. CDR1 and CDR2, pointing to methylation and mutations within these regions, (page 484, page 486, third and fourth paragraphs, page 487, last paragraph; Figures 1-2).

Regarding claims 5 and 6, Levy et al. shows regions of mutation in nucleic acid sequence that is nonsynonymous (CDR2 and CDR3) and synonymous (CDR1), (Figure 1; Tables 1-2).

Regarding claim 7, Levy et al. shows a table of single nucleotide polymorphisms for one or more nucleic acid sequences, (Tables 1-2).

Regarding claims 9-10, Levy et al. shows a table (dataset) of various V genes with known methylation at the cytosine residues, (page 484, page 486, third and fourth paragraphs, page 487, last paragraph; Figures 1-2; Tables 1-2).

Regarding claim 37, Levy et al. shows cDNA sequence of expressed human tumor V genes, (page 476, last paragraph; Figures 1-2).

Regarding claim 38, Levy et al. shows genomic sequence, (page 477, first paragraph of results).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to modify the method of predicting regional mutability in antibody V genes by Shapiro et al. with the analysis of mutational regions of V genes with known methylation sites by Levy et al., because the regions of nucleic acid with a tendency of mutation may be influenced by methylation of specific cytosine residues as shown by Levy et al., (page 487; Figures 1-2; Tables 1-2).

Claims 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over Shapiro et al. (Journal of Immunology, 1999, 163, 259-268) in view of Levy et al. (J. Exp. Med., 1988, 168, 475-489) as applied to claims 2, 3, 5-7, 9, 10 and 37 above, and further in view of Lippa et al. (American Journal of Pathology, 1998, 153(5), 1365-1370).

The instant claim 11 depends from claim 1 with the extra limitation that the dataset of two or more genes comprises a dataset of known mutation dataset.

Shapiro et al. and Levy et al. do not show a dataset of genes with known mutations.

Lippa et al. shows a dataset with genes with known mutations, (Table 1).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to modify the method of predicting regional mutability in antibody V genes by Shapiro et al. with the analysis of mutational regions of V genes with known methylation sites by Levy et al. and the use of a dataset of genes with known mutations by Lippa et al., because the regions of nucleic acid with a tendency of mutation may be influenced by methylation of specific cytosine residues as shown by Levy et al., (page 487; Figures 1-2; Tables 1-2) and a dataset of known mutations by Lippa et al. would allow one skilled in the art to distinguish gene regions of mutability with gene regions already known to contain mutations.

Claims 12 is rejected under 35 U.S.C. 103(a) as being unpatentable over Shapiro et al. (Journal of Immunology, 1999, 163, 259-268) in view of Levy et al. (J. Exp. Med., 1988, 168, 475-489) as applied to claims 2, 3, 5-7, 9, 10 and 37 above, and further in view of Reiter et al. (Genome Research, 2001, 11, 1114-1125).

The instant claim 12 depends from claim 1 with the extra limitation that the dataset of two or more genes comprises a dataset of known diseases.

Shapiro et al. and Levy et al. do not show a dataset of genes with known diseases.

Reiter et al. shows a dataset with genes with known mutations, (Table 2).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to modify the method of predicting regional mutability in antibody V genes by Shapiro et al. with the analysis of mutational regions of V genes with known methylation sites by Levy et al. and the use of a dataset of genes with known diseases by Reiter et al., because the regions of nucleic acid with a tendency of mutation may be influenced by methylation of specific cytosine residues as shown by Levy et al., (page 487; Figures 1-2; Tables 1-2) and a dataset of known mutations by Reiter et al. would allow one skilled in the art to assess potential results of mutatable genes and potential types of diseases.

Claims 13-21, 47, 48 and 52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shapiro et al. (Journal of Immunology, 1999, 163, 259-268) in view of Levy et al. (J. Exp. Med., 1988, 168, 475-489) as applied to claims 2, 3, 5-7, 9, 10 and 37 above, and further in view of Smigielski et al. (Nucleic Acids Research, 2000, 28(1), 352-355).

The instant claims 13-21, 47, 48 and 52 depend from claim 1 with the extra limitation that the dataset of two or more genes comprises a type of database.

Shapiro et al. and Levy et al. do not show a dataset of genes comprising a database.

Smigielski et al. shows a database of single nucleotide polymorphisms, (pages 352-353).

The only difference between the claimed invention and the teaching of Shapiro et al in view of Levy et al. and further in view of Smigielski et al. is the content of the database. The content of the database is nonfunctional descriptive material. The MPEP states in 2106 VI and 2106.01 in discussing computer related inventions in light of In re Gulack, 703 F.2d 1381, 1385, 217 USPQ 401, 404 (Fed. Cir. 1983):

VI. DETERMINE WHETHER THE CLAIMED INVENTION COMPLIES WITH 35 U.S.C. 102 AND 103

Reviewing a claimed invention for compliance with 35 U.S.C. 102 and 103 begins with a comparison of the claimed subject matter to what is known in the prior art. See MPEP § 2131 - § 2146 for specific guidance on patentability determinations under 35 U.S.C. § 102 and 103. If no differences are found between the claimed invention and the prior art, then the claimed invention lacks novelty and is to be rejected by USPTO personnel under 35 U.S.C. 102. Once differences are identified between the claimed invention and the prior art, those differences must be assessed and resolved in light of the knowledge possessed by a person of ordinary skill in the art. Against this backdrop, one must determine whether the invention would have been obvious at the time the invention was made. If not, the claimed invention satisfies 35 U.S.C. 103.

2106.01

*When nonfunctional descriptive material is recorded on some computer-readable medium, in a computer or on an electromagnetic carrier signal, it is not statutory and should be rejected under 35 U.S.C. 101. In addition, USPTO personnel should inquire whether there should be a rejection under 35 U.S.C. 102 or 103. USPTO personnel should determine whether the claimed nonfunctional descriptive material be given patentable weight. USPTO personnel must consider all claim limitations when determining patentability of an invention over the prior art. In re Gulack, 703 F.2d 1381, 1385, 217 USPQ 401, 403-04 (Fed. Cir. 1983). USPTO personnel may not disregard claim limitations comprised of printed matter. See Gulack, 703 F.2d at 1384, 217 USPQ at 403; see also Diehr, 450 U.S. at 191, 209 USPQ at 10. However, USPTO personnel need not give patentable weight to printed matter absent a new and unobvious functional relationship between the printed matter and the substrate. See ** Lowry, 32 F.3d **>at<*

*1583-84, 32 USPQ2d **>at< 1035 **; In re Ngai, 367 F.3d 1336, 70 USPQ2d 1862 (Fed. Cir. 2004).*

Common situations involving nonfunctional descriptive material are:

- a computer-readable storage medium that differs from the prior art solely with respect to nonfunctional descriptive material, such as music or a literary work, encoded on the medium,

- a computer that differs from the prior art solely with respect to nonfunctional descriptive material that cannot alter how the machine functions (i.e., the descriptive material does not reconfigure the computer), or

- a process that differs from the prior art only with respect to nonfunctional descriptive material that cannot alter how the process steps are to be performed to achieve the utility of the invention.

Thus, if the prior art suggests storing a song on a disk, merely choosing a particular song to store on the disk would be presumed to be well within the level of ordinary skill in the art at the time the invention was made. The difference between the prior art and the claimed invention is simply a rearrangement of nonfunctional descriptive material.

The difference between Shapiro et al in view of Levy et al. and further in view of Smigielski et al. and the claimed invention constitutes non-functional descriptive material because the content of the database does not alter how the method of predicting mutability in genes, i.e., the data in the database does not limit the claimed method to predict mutations differently than the method of Shapiro et al in view of Levy et al. and further in view of Smigielski et al. Therefore no patentable weight is given to the databases in the claimed method.

Claim 56 is rejected under 35 U.S.C. 103(a) as being unpatentable over Shapiro et al. (Journal of Immunology, 1999, 163, 259-268) in view of Levy et al. (J. Exp. Med.,

1988, 168, 475-489) and further in view of Smigielski et al. (Nucleic Acids Research, 2000, 28(1), 352-355) as applied to claims 13-21, 47, 48 and 52 above.

The instant claim 56 is analogous to the method claims 13-21, 47, 48 and 52, except the method is performed in silico.

In *In re Venner*, 262 F.2d 91, 95, 120 USPQ 193, 194 (CCPA 1958), the court held that broadly providing an automatic or mechanical means to replace a manual activity which accomplish the same result is not sufficient to distinguish over the prior art (see also *Manual of Patent Examining Procedure,* U.S. Trademark and Patent Office, section 2144.04, III).

In the instant case, the claimed invention merely makes the process of Shapiro et al., Levy et al. and Smigielski et al. performed in silico. Shapiro et al., Levy et al. and Smigielski et al. shows datasets comprising various databases which would include a human mutant database and a variation predictiveness matrix. It is thus not sufficient to distinguish over Shapiro et al., Levy et al. and Smigielski et al. Therefore, the claimed invention, i.e. the method of claims 13-21, 47, 48 and 52 wherein the step of generating the variation predictiveness matrix is performed in silico and the dataset of two or more genes comprises a human mutant database, would have been obvious to a person of ordinary skill in the art at the time the invention was made over the process disclosed by Shapiro et al., Levy et al. and Smigielski et al.

Furthermore, while Shapiro et al. does not explicitly disclose performing in silico the process as in claims 13-21, 47, 48 and 52, they do disclose that all unmutated germline sequences were manipulated and analyzed with MACVECTOR version 5.0

software, (page 260, left column, fourth paragraph). Thus they at least disclose a computer readable medium comprising instructions for executing at least steps of analyzing sequences. Thus, the entire method of Shapiro et al., Levy et al. and Smigielski et al. could be interpreted as semi-automatic. One of ordinary skill in the art would have been motivated to make it perform the method of claims 13-21, 47, 48 and 52 in silico to take the obvious advantage of a fully automatic process, i.e. saving time and cost.

There would have been a reasonable expectation of success because the court held regarding software that "writing code for such software is within the skill of the art, not requiring undue experimentation, once its functions have been disclosed." Fonar Corp., 107 F.3d at 1549, 41 USPQ2d at 1805.

Claims 53, 57, 203 and 204 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shapiro et al. (Journal of Immunology, 1999, 163, 259-268), as applied to claim 1 above.

The instant claims 53, 57, 203 and 204 are analogous to the method claim 1, except the method is effected by a computer program (claim 53), performed in silico (claim 57), drawn to a computer readable medium encoded with a computer program for predicting variations in a wild-type gene sequence (claim 203) or codons in a wild-type gene sequence (claim 204).

In *In re Venner*, 262 F.2d 91, 95, 120 USPQ 193, 194 (CCPA 1958), the court held that broadly providing an automatic or mechanical means to replace a manual

activity which accomplish the same result is not sufficient to distinguish over the prior art (see also *Manual of Patent Examining Procedure,* U.S. Trademark and Patent Office, section 2144.04, III).

In the instant case, the claimed invention merely makes the process of Shapiro et al. as a method effected by a computer program, performed in silico or as a computer readable medium with code and indeed accomplishes the same result. Shapiro et al. shows predicting mutability in wild-type gene sequences (unmutated sequence) and codons, (page 260, left column, fourth paragraph; Figure 7). It is thus not sufficient to distinguish over Shapiro et al. Therefore, the claimed invention, i.e. performing the method in silico or the computer readable medium comprising instructions to execute a process would have been obvious to a person of ordinary skill in the art at the time the invention was made over the process disclosed by Shapiro et al.

Furthermore, while Shapiro et al. does not explicitly disclose performing in silico or a computer medium comprising instructions for executing all the steps of the process as in claim 1, they do disclose that all unmutated germline sequences were manipulated and analyzed with MACVECTOR version 5.0 software, (page 260, left column, fourth paragraph). Thus they at least disclose a computer readable medium comprising instructions for executing at least steps of analyzing sequences. Thus, the entire method of Shapiro et al. could be interpreted as semi-automatic. One of ordinary skill in the art would have been motivated to make it completely automatic by performing the method in silico or comprising instructions in the computer readable medium for

executing all steps of the method to take the obvious advantage of a fully automatic process, i.e. saving time and cost.

There would have been a reasonable expectation of success because the court held regarding software that "writing code for such software is within the skill of the art, not requiring undue experimentation, once its functions have been disclosed." Fonar Corp., 107 F.3d at 1549, 41 USPQ2d at 1805.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to LARRY D. RIGGS II whose telephone number is (571)270-3062. The examiner can normally be reached on Monday-Thursday, 7:30AM-5:00PM, ALT. Friday, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie Moran can be reached on 571-272-0720. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Shubo (Joe) Zhou/
Primary Examiner, Art Unit 1631

/LDR/
Larry D. Riggs II
Examiner, Art Unit 1631

Shubo (Joe) Zhou, Ph.D.
Primary Examiner